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HISTOLOGICAL LESIONS OF MUSCLE IN DERMATOMYOSITIS. DIFFERENTIATION FROM RELATED MUSCULO-CUTANEOUS SYNDROMES.

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As we pointed out in 1953, it seems that the most has not been made of the histological examination of muscle in the study of the so-called "collagen diseases". This omission is perhaps to be attributed to the fact that most authors are satisfied if they can obtain microscopical confirmation of clinically presumed muscular involvement and do not pay sufficient attention to the anatomical changes and to the development of the lesions in time and extent. They have thus neglected the possibility of classifying histologically the various musculo-cutaneous syndromes.

It is certainly true as Bergouignan wrote in 1945, that "muscle is capable of only a limited range of reactions", but it is obvious that lesions of the surrounding supporting tissue containing vessels and nerves may diversify the basic histological picture.

Although the pathological process may primarily involve the muscle itself it is logical to assume that in other cases it may begin in the surrounding collagen or the associated vascular structures. Some writers, concentrating unduly on the muscle lesion, have proposed grouping together various disorders in which the muscles are involved. We consider it more logical to establish on histological grounds a more analytical classification of the heterogeneous groups already anticipated on clinical grounds.

Several disorders are characterized by a combination of cutaneous and muscular manifestations. One can differentiate clinically the dermatomyositis and the sclerodermas from acute lupus erythematosus with muscular involve-

ment and from periarteritis nodosa. In their purest forms confusion is hardly possible.

Dermatomyositis presents in its acute form as a severe disorder, usually febrile, characterized by extensive involvement of the striated muscles with muscle pain and functional weakness; and by a lilac "erythroedema" showing a predilection for the eyelids, the face and the extensor aspects of the joints; it is often fatal. In more favourable cases the condition assumes a chronic course with a reversible myositis and poikilodermatous cutaneous atrophy (poikilodermatomyositis of Petges and Jacobi). In some cases the cutaneous component is absent and the picture is then that of a polymyositis more familiar to the neurologists.

Muscular lesions may accompany both types of scleroderma. In scleroedema of Buschke, or oedematous scleroderma of Hardy, the muscles involved underlie the sclerodermatous area and may pass through all stages from simple functional weakness to oedematous infiltration and terminal atrophy which may or may not be followed by myosclerosis. In progressive scleroderma muscular involvement is a less constant feature. It often extends beyond the zones of scleroderma and ends in muscular atrophy which may be severe. In certain case reports one encounters a mixture of sclerosis and of poikilodermatous atrophy accompanied by diffuse muscular involvement. It is to these forms that we confine the term scleropoikilodermatomyositis.

The muscular lesions of acute systemic lupus erythematosus are often less conspicuous. They pass unnoticed in a severe general picture with multiple visceral manifestations (endocarditis, nephritis, lesions of the nervous system, polyserositis). The classic bat's-wing appearance, the violaceous lesions of palms and soles, are in direct contrast to the cutaneous manifestations of dermatomyositis, but the occasional predominant involvement of the muscles with relatively mild cutaneous and visceral lesions may cause confusion between the two conditions. Search for L.E. cells and for Hasegawa's factor is often useful.

Periarteritis, from the clinical point of view, rarely involves difficulty in diagnosis from the preceding conditions. The publications devoted to it in recent years and the value of muscle biopsy in diagnosis have induced us to include it in this study on the occasion of a recent case.

Although the typical forms of these conditions can hardly be confused, borderline cases are often encountered which are difficult or sometimes even impossible to classify—purely muscular forms of periarteritis nodosa, polymyositis without skin manifestations, oedematous sclerodermas, etc. Such cases explain the tendency of some authors to clump together these different syndromes in large artificial groups. We think this regrettable, for the detailed study of the histopathology of muscle offers a practical means of resolving these problems.

THE HISTOLOGY OF DEGENERATIVE CHANGES IN MUSCLE.

It is customary and logical to differentiate lesions of the muscle parenchyma from those of the interstitial tissue. In fact it is impossible to observe these types in absolutely pure form. The two processes are always closely interrelated with predominance of one or the other.

Parenchymatous myositis.—Muscle fibres may show various degenerative changes involving either the fibrils or the sarcoplasm or the two elements simultaneously. Degeneration of the fibrils is known as waxy degeneration of Zenker. One sees first the disappearance of transverse striation; part of the fibre is transformed into a homogeneous mass staining orange with eosin, later breaking up into more or less compact blocks recalling the beads of a rosary. If the sarcoplasm is intact one can observe proliferation of the nuclei and segmentation of the plasmodium into macrophagic cells which destroy the fragments of waxy substance and then, fusing together, reconstitute the primitive plasmodium. Fibrils reappear in this new part of the fibre and re-establish the continuity of the damaged element.

Degeneration of the sarcoplasm may present various appearances and naturally involves the disappearance of the fibrils. One may observe :

(i) Granular degeneration. The fibre is dotted with refractile granules of variable size and the nuclei show signs of pyknosis.

(ii) Vacuolar degeneration, characterized by the formation of large vacuoles which push the fibrils to one side and eventually destroy them.

(iii) Fatty degeneration may appear inside the fibre. This is one of the reactive phenomena of connective-vascular tissues; infiltration with serum and blood, cellular reactions and later sclerosis.

Interstitial myositis.—This is characterized by primary involvement of the interstitial tissue followed by more or less extensive destruction of the muscle fibres. One may meet various pictures according to whether the cellular reaction or the collagen reaction predominates. One may recall here the classical histological picture of Erb-Goldflam myasthenia, the characteristic groups of lymphocytes infiltrating the spaces between muscle bundles, formerly described by Buzzard as lymphorrhages.

It is on this basis of histopathology that we wish to orientate the study of our own cases.

In order to compare muscular lesions more accurately it is an advantage always to carry out the biopsies in the same region. Most authors consider the pectoral muscle most appropriate. The sections have been stained by haematoxylin-eosin, Dominici, iron haematoxylin, haemalum, Masson's trichrome and MacManus.

Rapid examination at low magnification may be misleading; the section must be studied at length and sometimes at high magnification if the details

of the various muscular degenerations are to be fully appreciated. In some of our cases the numerous nuclei might on superficial examination have been mistaken for lymphorrhages. With appropriate magnification one could establish that these nuclei were parts of muscle fibres emptied of their contents, transformed into hollow tubes and flattened one against the other. These "rosary" nuclei were all that remained of the fibre and formed almost homogeneous plaques.

The Dominici stain is an excellent procedure for cytological study, but proves less reliable than iron haematoxylin. The latter stain gives greater detail and contrast for the study of the various degenerations of the contractile elements.

CASE REPORTS.

CASE 1.—A man aged 50 (Joulia *et al.*, 1953a).

Acute dermatomyositis. Muscle biopsy (tibialis anterior) carried out in November 1949, two months after the onset of the disease. *Stain*: Haematoxylin-eosin and iron haematoxylin.

There is gross interfascicular oedema which also involves the muscle fibres. They appear irregularly swollen and their nuclei are arranged in "rosaries". Side by side with healthy muscle fibres which retain their striation are groups of fibres almost all the elements of which have assumed a homogeneous grey colour and from which all striation has disappeared. Some fibrils escape this degeneration and stand out in contrast to the general homogeneous grey background. Other fibres appear less seriously affected. They assume a waxy hair-like appearance and are invaded by vacuoles clear or with spongy contents. No interstitial reaction is detectable and the vessels appear normal.

In summary, the muscle appears very oedematous throughout. The histological changes indicate pure involvement of the muscle fibre which presents all the stages of degeneration from simple loss of transverse striation to complete waxy degeneration by way of the stage of vacuolation.

CASE 2.—A man aged 70 (Joulia *et al.*, 1953b).

Acute dermatomyositis. Muscle biopsy (pectoralis major) carried out in January 1951, two months after the onset of the disease. *Stain*: Iron haematoxylin.

The muscle lesions are considerable. One can make out all the stages of a progressive degeneration which destroys the muscle fibre and eventually empties it of its contents. It is first manifest by an oedematous swelling with disappearance of transverse striation then by vacuolar areas. Some fibres are invaded by granular or fluffy elements and are eventually transformed into a homogeneous waxy mass. Others, in contrast, completely emptied of their contents, can be recognized only by the presence of nuclei and remnants of sarcolemma.

The connective tissue is slightly oedematous and in it one finds a discrete infiltrate of lymphocytes and histiocytes with scanty plasma cells and polymorphonuclear cells.

CASE 3.—A man aged 62 (Joulia *et al.*, 1953c).

Acute dermatomyositis. Biopsy (pectoralis major) carried out in October 1951, three months after the onset of the disease. *Stains*: Haematoxylin-eosin. Iron haematoxylin.

The section is rather irregularly stained as a consequence of different degrees of degeneration of the muscle fibres. They appear oedematous throughout and creased as if too narrowly confined within their sheaths, losing their transverse striation. Some present a granular or even vacuolated and cotton-wool appearance. The nuclei

are increased in size and number. The interstitial tissue is infiltrated with oedema and there is some perivascular infiltration with lymphocytes and histiocytes.

CASE 4.—A woman aged 47 (Aubertin *et al.*, 1953).

Acute dermatomyositis. Biopsy (pectoralis major) carried out in November 1951, five months after the onset of the disease. *Stains*: Haematoxylin-eosin, saffron and iron haematoxylin.

The muscle fibres appear heaped one against the other. The clear spaces which can be detected at low magnification and which could be taken for interfascicular connective tissue are in fact complete bundles of lysed muscle fibres occupied by nuclei, often pyknotic, which are crowded together having lost their normal distribution. There is neither an infiltrate of lymphocytes and histiocytes between the bundles nor any reaction of the collagen. At high magnification few have retained their transverse striation and all stages of degeneration can be seen—the hair-like appearance, more or less gross vacuolisation, degeneration of granular or spongy or waxy type. Sometimes the fibres are completely emptied of their contents and only the coalescent nuclei can be found.

CASE 5.—A boy aged 5 (Berton, 1954).

Acute dermatomyositis. Biopsy (pectoralis major) carried out in 1953, three months after the onset of the disease. *Stains*: Haematoxylin-eosin. Iron haematoxylin.

The muscle bundles are separated by very lax connective-tissue spaces, very often infiltrated with oedema and less frequently with blood. There are neither interstitial cellular reactions nor vascular lesions. The muscle fibres appear unequal in size and irregularly stained. Numerous fibres, in no distinctive distribution, have lost their transverse striation and show granular vacuoles and sometimes even large plaques of waxy degeneration. There is no nuclear hyperplasia.

CASE 6.—A man aged 44 (Joulia *et al.*, 1953*d*).

Acute dermatomyositis, with transition to a chronic stage. Good response to cortisone. Biopsy (pectoralis major) carried out in February 1953, eight months after the onset of the disease, during the course of cortisone treatment. *Stains*: Haematoxylin-eosin. Iron haematoxylin.

Low magnification gives little information concerning muscular involvement. The staining in general appears fairly uniform; there are no lymphorrhages, the vessels are not dilated, and there is no significant interfascicular connective-tissue reaction. Higher magnification reveals lesions which are unquestionable but which must be sought among fibres which have retained their structure. One sees here and there occasional elements with numerous swollen nuclei; the limits of the fibre are blurred, its centre is spongy and occupied by large vacuoles, which sometimes coalesce. Other fibres are reduced to narrow ill-defined strands which disappear in the midst of surrounding healthy muscle elements. In places the lesions are less sparse and entire bundles of muscle fibres are poorly stained, appear swollen with oedema, and have partly lost their transverse striation.

CASE 7.—A man aged 68 (Joulia *et al.*, 1956*b*).

Acute dermatomyositis. Biopsy (pectoralis major) carried out in July 1955, two months after the onset of the disease. *Stains*: Toluidine blue and iron haematoxylin.

Only scanty changes are present. The affected fibres are difficult to discover in the midst of apparently normal muscle bundles. They have lost their transverse striation and present a hair-like appearance with vacuolar degeneration. Numerous apparently healthy muscle fibres are already swollen with oedema. Throughout, the nuclei are increased in number. In transverse section the lesions are much more striking. The fibrils appear pushed to the periphery of the fibre by oedema and are sometimes replaced by large clear vacuoles. There is no lymphocytic infiltrate and the vessels appear normal although dilated and gorged with blood.

In summary, the pathological changes are remarkably localized. They consist essentially of oedema and of the isolated involvement of muscle fibres without interstitial reaction. It is probable that these are the primary changes of the disease.

CASE 8.—A man aged 45 (unpublished case from the Medical Clinic of Professor Aubertin).

Acute dermatomyositis in a patient with cancer of the larynx. Skin biopsy (thigh) carried out in April 1956, one month after the onset of the disease. *Stains*: Dominici and iron haematoxylin.

The epithelium is essentially normal in appearance. The dermis is invaded throughout its extent by groups of histiocytes, particularly around the dilated vessels.

The attention is attracted by the presence of "arrectores pilorum" muscles cut longitudinally. The nuclei are swollen and irregular. In some fields the limits of the smooth muscle fibres are indefinite and the fibres appear vacuolated or granular and recall the lesions of striated muscle in dermatomyositis.

CASE 9.—A woman aged 29 (Texier, 1950).

Subacute dermatomyositis. Biopsy (biceps) carried out in March 1941, eight months after the onset of the disease. *Stains*: Haematoxylin-eosin and iron haematoxylin.

The muscle bundles are widely separated by dense connective tissue rich in fixed cells and in large lymphocytes and plasma cells. This connective tissue penetrates even between the muscle fibres which it seems to strangle as it becomes organized. The vessels are dilated. The connective-tissue reaction is accompanied in places by large collections of lymphocytes and histiocytes in immediate contact with the muscle fibres (true lymphorrhages).

The very characteristic mosaic appearance is seen in transverse sections: fibres are completely emptied of their contents and retain only a few centrally placed nuclei. In others the fibrils are pushed to the periphery or to the centre by the large granular vacuoles. Others are completely invaded by a homogeneous serous degenerative substance.

CASE 10.—A girl aged 16 (Joulia *et al.*, 1953e).

Subacute dermatomyositis. Biopsy (pectoralis major) carried out in September 1952, six months after the onset of the disease. *Stains*: Toluidine blue and iron haematoxylin.

The muscle bundles are separated by slight oedema and by massive extravasations of blood. The lesions tend to be grouped. Normal fibres are surrounded by others which have completely degenerated. The latter at first appear swollen by oedema and assume a spongy appearance. Others are vacuolated and sometimes end abruptly like stumps. They sometimes assume a beaded appearance as the result of the juxtaposition of different degrees of degeneration, from simple disappearance of transverse striation to vacuolation and homogeneous waxy degeneration. The interfascicular connective tissue is delicate and sometimes scattered with clusters of lymphocytes and histiocytes; this occurs particularly around the vessels which are dilated and gorged with blood and show thickening of their connective tissue sheath.

To summarize, this section shows, side by side with the clinical lesions of the muscle fibre, interstitial infiltrates of lymphocytes and histiocytes and, most strikingly, an abundance of extravasated blood infiltrating between the bundles and even between the muscle fibres. Its distribution makes it possible to exclude a biopsy artefact and it apparently corresponds to the so-called haemorrhagic form of Prinzing.

CASE 11.—A girl aged 17 (Joulia *et al.*, 1953f).

Subacute dermatomyositis. Biopsy (pectoralis major) carried out in July 1953, five months after the onset of the disease. *Stains*: Toluidine blue and iron haematoxylin.

The muscular lesions are considerable and entire muscle bundles have completely degenerated. The fibres have lost their normal structure and can be recognized only by the line of the nuclei which are often swollen and sometimes pyknotic. Transverse striation has disappeared and the fibres are invaded by vacuoles or by homogeneous waxy masses stained yellow by eosin. In some fields the sarcoplasm has completely disappeared and only the nuclei and remains of sarcolemma can be found.

In these zones of degeneration are large macrophagic cells which appear to destroy the remains of the fibrils. In other areas there is scanty interfascicular infiltrate of lymphocytes and histiocytes. The vessels are numerous, dilated and gorged with blood.

CASE 12.—A woman aged 48 (unpublished case from the Medical Clinic of Professor Creyx).

Subacute dermatomyositis of the arthropathic type. Biopsy (pectoralis major) carried out in July 1954, six months after the onset of the disease. *Stains*: Toluidine blue and iron haematoxylin.

There is gross oedema separating the muscle bundles. This gives a reticulated appearance to the interfascicular connective tissue which is scattered with sparse lymphocytes and histiocytes. There are numerous vessels with thickened walls. The oedema infiltrates the muscle fibres which appear swollen and heaped one against the other, sometimes assuming a cerebriform appearance. The lesions of the muscle fibres are extensive and grouped. The entire muscle bundle may be completely degenerated, showing in it vacuolated lesions progressing to complete waxy degeneration. At times the fibre is entirely emptied of its contents and is recognizable only by the persistence of the nuclei.

CASE 13.—A woman aged 22 (Joulia and Le Coulant, 1946).

Poikilodermatomyositis cured after treatment with glandular extracts and antergan. Biopsy (biceps) carried out in March 1942, several years after the onset of the disease. *Stains*: Haematoxylin-eosin and iron haematoxylin.

The gross reaction of the interfascicular connective tissue is striking. In places this tissue is oedematous, its delicate fibres separated, and there are large vessels gorged with blood. Elsewhere the connective tissue is dense and infiltrates deeply between the fibres accompanied by numerous lymphorrhages composed of lymphocytes and histiocytes. The muscle fibres are also profoundly affected; loss of transverse striation, oedema, vacuolar degeneration and even waxy degeneration give the impression of homogeneous formless tubes. In places the connective tissue and the lymphorrhages penetrate the muscle bundles so intimately that all differentiation is impossible. This connective tissue appears to be replacing the degenerated muscle.

CASE 14.—A man aged 76 (Le Coulant and L'Epee, 1947).

Poikilodermatomyositis in a patient with prostatic disease. Biopsy (biceps) carried out in August 1946, six months after the onset of the disease. *Stains*: Haematoxylin-eosin and iron haematoxylin.

The muscle bundles are separated by thick connective-tissue strands invaded by very dense infiltrates rich in lymphocytes and constituting true lymphorrhages. These cells infiltrate even within the bundles, between the muscle fibres which are themselves separated by oedema. The fibres appear swollen, stain poorly and lose their transverse striation. Some are vacuolated; others are homogeneous, staining metachromatically a yellowish-pink colour and undergoing waxy degeneration; others, finally, are emptied of their contents and identifiable only by their nuclei.

CASE 15.—A man, aged 48 (Broustet and Bergouignan, 1953).

Poikilodermatomyositis of Petges-Jacobi of melanodermic type. Muscle biopsy (biceps) carried out in April 1948, three years after the onset of the disease. *Stains*: Haematoxylin-eosin and iron haematoxylin.

The connective-tissue spaces between the bundles are enlarged but there is no fibrous hyperplasia. There are bands of oedema, thick strands of lymphocytes and histiocytes often centred around a vessel, infiltrating between the muscle fibres. These fibres stain very unequally, some being paler than their neighbours; transverse striation is generally absent; the majority appear swollen and some fibres show complete waxy degeneration.

CASE 16.—An infant of six months (unpublished case, Dr. Imbert, St. Quentin).

Oedematous scleroderma. Muscle biopsy. *Stains*: Haematoxylin-eosin and iron haematoxylin.

The muscle fibres are literally drowned in strands of dense collagen amongst which are fixed connective-tissue cells and a few lymphocytes. The collagen enters into contact with the stumps of muscle fibres which it appears to replace. It is sometimes difficult to know where muscle begins and collagen finishes. The muscle fibres are separated by slight oedema. There is considerable proliferation of the nuclei arranged in rosaries along the fibres. The latter have almost completely retained their striation.

CASE 16.—A man aged 25 (Aubertin and Labadie, 1953).

Oedematous scleroderma with muscle involvement. Biopsy (biceps), carried out six months after the onset of the disease, in December 1952. *Stains*: Haematoxylin-eosin and iron haematoxylin.

At low magnification an abundance of lymphorrhages can be seen progressively infiltrating the interfascicular spaces in closely packed groups, followed by the proliferation of thick strands of dense collagen. With a higher magnification one can make out in places streams of lymphocytes and histiocytes infiltrating the interfascicular spaces. The fibres here appear nibbled away or dissolved and replaced by dense collagen, but without the initial vacuolar or spongy degeneration seen in dermatomyositis. Absence of striation can be noted in the neighbourhood of the lymphorrhages. The nuclei in contrast are increased in size and number and arranged in rosaries. The diffuse infiltrate of histiocytes and lymphocytes shows no special perivascular distribution. The vessels appear normal.

CASE 17.—A man aged 45 (Texier, 1950).

Progressive scleroderma, with muscle involvement. Biopsy (biceps) carried out in May 1950, four years after the onset of the disease. *Stains*: Haematoxylin-eosin and iron haematoxylin.

The muscle bundles are widely separated by sheets of young collagen, which penetrates the interstices of the fibres. In this collagen are bands of lymphocytes and a few histiocytes. Among these cells can be found sparse sarcoplasm nuclei, like foreign bodies. This infiltration by collagen and lymphocytes seems to destroy the muscle fibres in the absence of any degenerative changes. The fibres have indeed preserved their longitudinal and transverse striation. Although in some places the fibres are overwhelmed and broken up in the young collagen, their normal striation can still be made out. This is no vacuolar or waxy degeneration.

CASE 19.—A woman aged 32 (Bonnin *et al.*, 1952).

Scleropoikilodermatomyositis. Biopsy (biceps) carried out in December 1951, seven months after the onset of the disease. *Stains*: Haematoxylin-eosin and iron haematoxylin.

The muscle bundles are very widely separated by strands of connective tissue which are more or less dense and are relatively acellular. They penetrate the interstices of the muscle fibres. At some places staining properties are altered: The red (muscle tissue) assumes imperceptibly a yellow tint corresponding to the collagen which follows the destruction of muscle. The nuclei are normal in quantity. The muscle fibres in general preserve their usual striation, but few appear homogeneous and are already scattered with yellowish areas as if invaded by collagen. The vessels are dilated and filled with blood.

CASE 20.—A woman aged 40 (Creyx *et al.*, 1953).

Systemic lupus erythematosus with muscular involvement. Biopsy (pectoralis major) carried out in January 1953, several years after the onset of the disease. *Stains*: Haematoxylin-eosin and iron haematoxylin.

In general the muscle appears little affected. One can find only a very definite increase in the number of nuclei which are arranged in rosary fashion. The muscle bundles are separated by gross oedema and in places the fibres themselves are swollen and wrinkled but show no signs of degeneration. They retain their transverse striation. The vessels are dilated and gorged with blood and are surrounded by a sheath of lymphocytes and histiocytes resembling the dermal infiltrate.

CASE 21.—A woman aged 35 (unpublished case of the Medical Clinic of Professor Creyxx).

Systemic lupus erythematosus with muscular involvement. Biopsy (pectoralis major) carried out in October 1955, six months after the onset of the disease. *Stains*: Toluidin blue and iron haematoxylin.

The muscle bundles are separated by oedema and often by haemorrhages. The interfascicular connective tissue septa are much thickened and contain numerous dilated vessels surrounded by prominent infiltrates of lymphocytes and histiocytes. In other places the vessels show a swollen endothelium and the cells of the infiltrate seem to penetrate their walls. A few vessels are thrombosed.

The muscle fibres appear practically normal. They have retained their striation and homogeneity. One can, however, detect slight oedema and some proliferation of the nuclei.

CASE 22.—A woman aged 32 (Joulia *et al.*, 1956a).

Periarteritis nodosa with mutilating gangrenous manifestations. Histological examination of the right extensor digitorum brevis muscle made in September 1955 from amputation material two years after the onset of the disease. *Stains*: Haematoxylin-eosin.

The muscle bundles are very distinctly separated by marked oedema which enables one to distinguish delicate collagen becoming condensed around the vessels; this is later invaded by very numerous lymphocytes and histiocytes infiltrating the walls of the vessels with the result that they appear much thickened. The small calibre vessels show endarteritis, sometimes resulting in obliteration of the vascular lumen. The muscle lesions are poorly defined and consist of oedema of the muscle fibre which is wrinkled as if too narrowly confined within its sheath through which it sometimes bursts. The transverse striation may disappear but there is no vacuolar, granular or waxy degeneration. The muscle lesions are definitely more marked in the neighbourhood of the vessels.

A detailed study of our case reports thus permits one to form a picture of the muscle lesions in dermatomyositis, scleroderma, acute systemic lupus erythematosus and periarteritis nodosa.

DERMATOMYOSITIS.

Oedema is the essential lesion, involving both the connective tissue and the parenchyma; the fibres are swollen in irregular groups and are sometimes heaped one against the other. When oedema in the muscle predominates the fibrils assume a corrugated appearance as if they were too narrowly confined within their sarcoplasmic sheath.

The muscle parenchyma.—It is difficult to distinguish the lesions of the sarcoplasm from those of the contractile elements. They usually co-exist to the point of merging. Attention must first be drawn to the variation in the volume of the muscle fibres and the variable degree to which they are involved even in the same element or in a single group of fibres. One may in fact see side by side disappearance of transverse striation, granular degeneration of entire fibres or of fragments of fibres, waxy acellular blocks, sometimes segmented, staining orange with eosin and grey-blue with Dominici. Vacuoles of various sizes may occupy an entire fibre literally emptied of its contents and reduced to its sarcolemma. Proliferation of the nuclei is regularly present;

they are increased in size, reticulated, arranged in a rosary and showing no mitosis. One sometimes has the impression of ghost fibres containing only the debris of pyknotic nuclei. In some cases one may see single or multinucleated macrophages which seem to destroy the acellular debris of waxy degeneration (Case 10). In the midst of this picture of destruction it is possible to see the persistence of certain fibrils in a degenerating fibre and even stumps of fibres spared by the attack. In transverse section the lesions are equally instructive and present the classical "mosaic" appearance.

The interstitial lesions.—Oedema is the essential change; it is sometimes accompanied by an infiltrate of cells, particularly histiocytes and lymphocytes; but it is not uncommon to find plasma cells and occasionally eosinophils, scattered along the fibres and not concentrated around the blood vessels. The classical descriptions have laid great emphasis on the lymphorrhages described by Buzzard in myasthenia. In our opinion they are much less common and less important than has been maintained except in slowly progressive cases.

When it is present, sclerosis is arranged in more or less dense strands infiltrating the degenerating muscle fibres. It is then practically impossible, even with special stains, to distinguish the remains of degenerate muscle fibres from connective tissue. The presence of numerous nuclei is difficult to interpret; one would be tempted at low magnification to consider them as purely exogenous infiltrates but on more detailed examination they can be shown to be partly the nuclei of muscle fibres undergoing destruction. This finding sometimes allows a different interpretation to be placed on the so-called lymphorrhages of earlier authors. The vessels show only insignificant changes. In some cases there are interfascicular haemorrhages which may be evidence of marked capillary fragility (haemorrhagic form of Prinzing, Case 10).

We made no special staining of the nerves but according to those who have studied this matter the nervous networks and the nerve endings are normal. We would draw attention in passing to the curious lesions of the arrectores pilorum muscles in Case 8.

We should emphasize the wide diversity of the lesions from one patient to another and also their polymorphism in a single section; but if the age of the patient and the clinical form of the disease are borne in mind it is possible to attempt a chronological assessment of the histological findings.

(a) *In very acute forms* (biopsy carried out two months after the onset, Cases 1, 2, 7), there are only parenchymatous lesions in an oedema which is usually marked. It sometimes required minute and determined examination to discover lesions localized to a few fibres or fragments of fibres. One may, on the contrary, observe the massive gangrene of an entire bundle of fibres without any reaction of the interstitial tissue.

(b) *In the more chronic forms* (biopsies carried out 3-6 months after the onset, Cases 4, 10, 11) there is a more marked and more diffuse extension of the degeneration which makes the diagnosis obvious at a glance. At this period the muscle fibres, emptied of their contents, are represented only by the sarcolemma and the nuclear rosaries which define their outline. The cellular reaction becomes defined and one can distinguish two components: first, proliferation of the nuclei, segmentation of the sarcoplasm and formation of macrophages which attack the waxy blocks of Zenker; and second, the appearance of infiltrates, still discrete, which insinuate themselves into the interstitial spaces.

(c) It is only in the more advanced forms (Cases 13, 14, 15) that the classical picture appears in its complete form.

The parenchymatous lesions have hardly changed but in contrast the interstitial reaction is more intense: Lymphorrhages in dense sheets infiltrating and separating bundles and fibres, the disappearance of the macrophages and the appearance of increasing quantities of collagen, replacing the remnants of degenerated fibres, and evidence of the myosclerosis which is clinically apparent.

In brief, one notes consecutively oedema and death of the fibre, its degeneration, and the much later interstitial reaction both cellular and connective tissue.

THE SCLERODERMAS.

Whether it is a question of the oedematous forms or of the progressive type, the histological picture is the same. The dominant feature is interstitial, consisting of dense cellular plaques of lymphocytes and histiocytes separating and infiltrating bundles and fibres followed by collagen strands. The parenchyma is involved only by contact with these strands and in proportion to their invasion. Sometimes one may even come across isolated fragments of fibres which have escaped the degenerative process and survive within the invading mass of collagen.

ACUTE SYSTEMIC LUPUS ERYTHEMATOSUS.

The study of the muscular lesions is full of interest because it allows one to differentiate by muscle biopsy controversial cases which cannot clinically be differentiated from dermatomyositis. The lesions here are much more discrete. In the midst of relatively slight oedema interstitial reactions predominate: Dilatation of the vessels with slight thickening of the walls, a perivascular infiltrate consisting mainly of lymphocytes with perhaps the beginnings of fibrinoid degeneration, and slightly excessive collagen. These lesions recall the general histological picture of acute systemic lupus erythematosus. The parenchyma is involved only secondarily by contact with these primary changes; oedema, a corrugated appearance of the contractile elements, and

the disappearance of transverse striation are the only evidence of pathological change.

PERIARTERITIS NODOSA.

Here the histological picture is dominated by the vascular lesion. Very large arteries may be seen with walls thickened and infiltrated with cellular elements with at times endarteritis, thrombosis and fibrinoid degeneration of collagen. The infiltrate diffuses into the more or less oedematous interstitial tissue. There are only minimal lesions of the muscular parenchyma—oedema, disappearance of transverse striation, and corrugation of the fibrils in contact with the vascular lesions.

CONCLUSIONS.

There are three types of pathological change which may be differentiated as a result of this study :

In lupus erythematosus and periarteritis the lesions are centred on the vascular element and seem logically to link up with an allergic pathology towards which current concepts of this disease are becoming orientated.

In contrast, the scleroderma pattern falls clearly into what it is conventional to call " collagen disease ".

The basic histology of dermatomyositis, which is centred round the preponderant primary lesion of the muscle parenchyma, direct research towards an autonomous disease of muscle, perhaps of virus origin.

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 ———, ———, DAVID-CHAUSE, TEXIER, BRABEN and FRUCHARD (1956a) *Ibid.*, **63**, 202.
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TINEA CRURIS IN WOMEN.

A REPORT OF THREE CASES.

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" I BELIEVE wives may and do take the disease, and use the same treatment as the husband, whilst the facts are concealed for very obvious reasons from the medical man." So wrote Tilbury Fox (1878) in a paper which records a family epidemic of "eczema marginatum" involving the father, three sons, a daughter, a valet and a male visitor. The diagnosis was confirmed by finding the mycelium in scales from the lesions. This is the earliest record of tinea cruris in the female which we have been able to discover. The next is by Perrin (1896) who gave clinical descriptions of tinea cruris in two female patients. Lastly, Malherbe (1920) and Aronstam (1922) also reported this disease in the female.

A careful search through British, French, German and American literature published since 1879 has yielded only five articles describing or recording tinea cruris in women where the clinical diagnosis was confirmed by culture. Nicolau (1913) recorded 5 female cases in a series of 29 attributable to *Epidermophyton floccosum*, of which 3 were apparently conjugal infections: de Mello (1921) isolated this fungus from groin lesions in an unspecified number of female European immigrants in Portuguese India; Photinos (1928) isolated it from a woman of 61 years. Silva, Keston and Benham (1955) recorded *Trichophyton rubrum* infection of the groin in a negress who presented with numerous lesions due to this fungus in other sites; lastly, Georg, Hand and Menges (1956) referred to tinea cruris due to *E. floccosum* in a woman.

Despite this paucity of published records, some text-books and monographs (Becker and Obermayer, 1947; Degos, 1953; Vanbreuseghem, 1954; Andrews, 1954; Ormsby and Montgomery, 1954) infer that, although tinea cruris is more frequent in the male it is at least not a rarity in the female. In others (Conant, 1955; Lewis and Hopper, 1948; Lutz, 1951; Simons, 1956; and Swartz, 1953) its incidence in women is not even mentioned. On the other hand, Ingram and Brain (1957) state that it is rare in women except in the tropics, and according to Pillsbury, Shelley and Kligman (1956) "it is relatively uncommon in females".

In our experience, women rarely report to skin clinics with this condition, 2 cases having been seen in Bristol in 2 years and one in Leeds in 7 years; two other cases based on strong presumptive evidence, but without confirmation by culture, were discovered by English (1957) in the course of a special investigation.

CASE REPORTS.

CASE 1.—A housewife aged 57.

History.—Maceration of skin with itching between the toes had been present for about 5 years. Four months before attending the skin clinic an itchy rash was noticed in the groin. Neither the patient nor her husband had travelled abroad beyond Europe.

On examination.—A red scaling area with a well-defined lower margin on the inner aspect of the upper part of the left thigh was seen. The labia and mons pubis were not involved. Slight maceration between the toes was also present.

Mycology.—Hyphae were found in scrapings from both groin and interdigital lesions and *T. rubrum* was isolated in culture from both sites. On Sabouraud test and preservation media the surface growth was white and floccose and on Sabouraud test medium a purplish red pigment was produced on the reverse side of the slope. On microscopic examination of the surface growth only pear-shaped to oblong microconidia on sparsely distributed pseudo-grappes and thyrses were observed. In the submerged growth some laterally-projecting intercalary chlamydospores with dense contents staining deeply in cotton blue were present. No macroconidia were seen.

CASE 2.—A housewife aged 44.

History.—A rash had first been noticed on the hand 7 years previously. This spread to include the face, forearms, groins and feet. The groins had been involved for about 1 year. She had never been abroad and the condition was first noticed several years before her marriage.

On examination.—Patches of scaling erythema were found in the areas mentioned; there was maceration between the toes and the toenails were discoloured. The groin lesions did not extend to the mons pubis or labia.

Mycology.—Scrapings from the hands, feet, toenails and groin showed fungal hyphae on microscopic examination, and on culture *T. rubrum* of the same type as Case 1 was obtained.

CASE 3.—A woman aged 47.

History.—Suffered from athlete's foot for 20 years prior to the appearance of present groin lesion, which followed a scald of the area. Recently returned from the Barrier Reef in Australia.

On examination.—Dusky discoloration with slightly scaling serpiginous border, including the inner aspect of both upper thighs, labia majora and mons.

Mycology.—Scrapings from the borders of the lesion on the mons and upper thighs revealed mycelium. Culture on Sabouraud's test and preservation media yielded *T. rubrum* showing the same macroscopic and microscopic features as were observed in the strains isolated from Cases 1 and 2.

DISCUSSION.

All these 3 cases are due to infection by *T. rubrum*. It seems probable that this is a reflection of the very marked rise in the incidence of *T. rubrum* infections in recent years, and the relative decline in the incidence of *E. floccosum* infections. Although some records of *T. rubrum* infection of the groin

appeared in the literature prior to 1928 (Bang, 1910; Ota and Kawasaki, 1922) most cases of tinea cruris in men and all in women were said to be caused by *E. floccosum*. Since then *T. rubrum* has become at least equally if not more important as the aetiological agent of this disease.

One source of infection for tinea cruris is probably an autogenous one, such as a tinea pedis lesion. This could account for the preponderance of tinea cruris in the male since the experience of others, as recorded in the literature, as well as our own in Bristol and Leeds, compel one to the conclusion that there is a greater incidence of tinea pedis in men than in women. But as Table I shows, it is only in the case of *T. rubrum* infection that such a correlation occurs with any frequency and this appears to be substantiated by general experience. *T. mentagrophytes* relatively rarely causes tinea cruris (according to Pillsbury, Shelley and Kligman (1956) this is frequent) although it is often the cause of tinea pedis; conversely, *E. floccosum* infection, which prefers the groin, is relatively rare in tinea pedis.

TABLE I.—Tinea Pedis and Tinea Cruris: combined figures for Bristol and Leeds for the two-year period 1954–1955

Fungus.	Tinea cruris only.			Tinea pedis with Tinea cruris.			Tinea pedis only.			Total number		
	Number of patients.			Number of patients.			Number of patients.			Number of patients.		
	Females.	Males.	Total.	Females.	Males.	Total.	Females.	Males.	Total.	Females.	Males.	Total.
<i>T. rubrum</i>	0	5	5	3	15	18	27	53	80	30	73	103
<i>T. mentagrophytes</i>	0	0	0	0	1	1	16	39	55	16	40	56
<i>T. r. interdigitale</i>												
<i>E. floccosum</i>	0	11	11	0	4	4	2	11	13	2	26	28

Table I also shows that *T. rubrum* infection in both tinea pedis and tinea cruris is much more frequent in men than in women. This might possibly be due to some intrinsic biochemical difference connected with sex, but the more likely explanation is probably that men are more often exposed to infection as for instance in the services, especially when abroad, and in the mining industry. Data obtained during the small familial survey previously referred to (English, 1957) show an almost equal incidence of tinea pedis and tinea cruris in the two sexes, and therefore tend to confirm this view as well as upholding the thesis of Tilbury Fox quoted at the beginning of this article.

Our thanks are due to Dr. R. P. Warin and Dr. C. D. Evans and to Dr. J. T. Ingram for permission to publish their cases and for helpful criticism.

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KERATOSIS FOLLICULARIS SERPIGINOSA (LUTZ). ELASTOMA INTRAPAPILLARE PERFORANS VERRUCIFORME (MIESCHER).

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KERATOSIS FOLLICULARIS SERPIGINOSA (K.F.S.) was the name used by Lutz to describe a curious chronic dermatosis when he recorded a case in 1952. Two further clinically identical cases were later reported by Ruiter and Beening (1955) and by Miescher (1955) and a third by Marshall and Lurie (1956). Miescher made a very careful study of the histological changes and suggested that the condition should be described as elastoma intrapapillare perforans verruciforme. Since the preparation of the report on our first case Ruiter (1956) has discussed his case in the light of Miescher's findings and Miescher (1956) has reported a case clinically suggestive of Kyrle's disease (hyperkeratosis follicularis et parafofollicularis in cutem penetrans) but showing histological changes like those in K.F.S.

The clinical picture in the few reported cases of K.F.S. (Miescher's second case (1956) excepted) is of circinate or arcuate peripherally spreading lesions on the nape and sides of the neck in children. The primary lesion is a little, grey, conical, keratotic papule, 2-3 mm. across, and lesions may be solitary or arranged from the first in rows or segments of circles. Some papules persist unchanged or enlarge only a little, others enlarge to about 5 mm. in diameter and present a rough, greyish, elevated edge with a central keratinous plug. Further spread leads to loss of the plug, central atrophy and the appearance of a border consisting of closely-set papules.

The picture in an established case is of discrete small and larger papules as described above and circinate, arcuate or serpiginous lesions consisting of keratotic ridges enclosing areas of atrophic-looking skin. At the base of the keratotic border the skin is pink to dusky red and the border itself consists of individual papules each with a central adherent keratotic plug which, when removed, leaves a crater-like depression. Peripheral spread occurs until the rings reach 15-20 mm. diameter. Spontaneous healing does not seem to occur. Keloidal scarring followed biopsy excision in both of our cases ; in the first it was of marked degree.

CASE REPORT

The patient, an otherwise healthy boy of 13 years, was brought for investigation of "ringworm" of his neck which had been present for at least 18 months. The lesions were said to have appeared shortly after an attack of impetigo. No other member of his family suffered from any skin disease.

On the nape and sides of the neck were several ringed and arcuate lesions together with scattered, discrete, small papules. Just within the scalp margin there was a large papule with a horny central plug. The minute appearance was exactly as described above and there was no hesitation in making a clinical diagnosis of K.F.S. No change in the appearance of the lesions occurred over a period of three months.

Histopathology.—A biopsy was taken from one of the rings. The specimen was fixed in formalin and embedded in paraffin wax. Serial sections were cut at 6 μ and

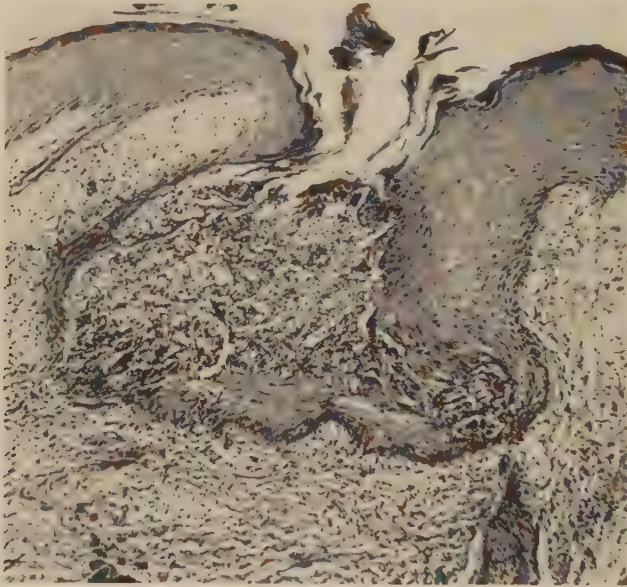


FIG. 1.—H. & E. $\times 75$.

stained with haematoxylin and eosin. A few sections were stained for elastic tissue with Verhoeff's stain.

Examination of these sections showed that the biopsy included two complete lesions and part of a third. All three showed essentially similar features, varying only in size.

The epidermis surrounding the lesion is hyperkeratotic and acanthotic (Fig. 1). The macroscopic papule consists of a localized area of hyperplasia of the epidermis which is traversed by a channel containing a mass of tissue which projects above the surface of the skin producing the keratotic plug. This channel communicates directly with the dermis, the point or points of communication being situated on the side of the epithelial mass. It courses through the epidermis in a somewhat zig-zag or spiral fashion. The track is lined in its upper third by parakeratotic stratum corneum and in its middle and lower thirds by degenerate, desquamating prickly cells. The plug itself consists in its upper third of parakeratotic horn lamellae and nuclear debris. In its middle and lower thirds it consists mainly of amorphous

basophilic debris, embedded in which are fragments of nuclear material and polymorphonuclear leucocytes. In addition in its middle third there are also some desquamated squamous cells, and in its lower third there are thick branching fibres with an eosinophilic core and a thin basophilic sheath. Some of them have basophilic cross striations. Many of these fibres are directly continuous with thick eosinophilic collagen bundles in the dermis.

In the subjacent and surrounding dermis there is a well-marked fibroblastic and foreign body giant cell reaction. Elastic tissue stains (Fig. 2) reveal a marked increase in positively staining material in the mid-dermis and in the papillae around the lesion. There is also a mass of "elastic" tissue extending from the dermis into the lower third of the intra-epithelial plug.

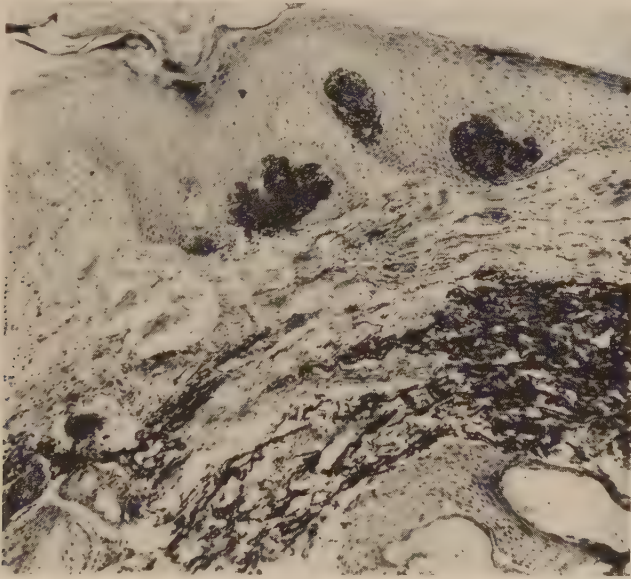


FIG. 2.—Verhoeff's stain. $\times 75$.

In two of the lesions hair follicles can be seen to traverse the epithelium forming the wall of the channel containing the "keratotic plug" but in neither case could a direct communication be demonstrated.

DISCUSSION

Miescher considers the primary pathological process to be the formation of an intrapapillary elastoma. Necrobiosis of this altered tissue is followed by its extrusion through the epidermis with attendant acanthosis, hyperkeratosis and parakeratosis.

We have, in discussing our first case, disputed this theory suggesting that the "elastoma" is, in fact, altered collagen and that the primary lesion is the rupture of hair follicles (due perhaps to ingrowing lanugo hairs) and possibly sweat ducts. Study of our second case neither confirms nor denies this theory.

The clinical appearances of K.F.S. may suggest either porokeratosis (Mibelli) or Kyrle's disease. Porokeratosis is easily excluded by histological examination but Kyrle's disease presents more difficulties especially in view of the findings in Miescher's second case (1956). This case presented papular, horny and atrophic lesions of the extensor surfaces of the limbs, with elective sites at knees and elbows, clinically similar to those of Kyrle's disease. The histological picture however was like that seen in K.F.S. We have, in reporting our first case, discussed the differential diagnosis of K.F.S. and Kyrle's disease and noted that the distribution of lesions in the two diseases is different and that the histopathological pictures, judging from the descriptions of typical cases in the literature, are not comparable. We noted, too, that de Graciansky *et al.* (1955), in reviewing the recorded cases of Kyrle's disease, rejected what was probably the first reported case (Fischer, 1927) of K.F.S. The question whether Miescher's second case is one of Kyrle's disease or one of disseminated K.F.S. must remain open until more cases of Kyrle's disease have been thoroughly investigated.

SUMMARY.

The clinical and histological findings in a second South African case of keratosis follicularis serpiginosa are presented.

The literature is briefly reviewed and the question of the relationship of K.F.S. to Kyrle's disease is discussed.

We are indebted to Dr. F. A. Brandt and Mr. M. Ulrich of the South African Institute for Medical Research, Johannesburg, for technical assistance and for the photomicrographs.

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TRAUMATIC MARGINAL ALOPECIA. A SPECIAL TYPE : ALOPECIA GROENLANDICA.

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DURING the past year we have seen 11 patients with traumatic hair loss of identical type. All were girls ranging in age from 8 to 18 and all did their hair in the modern teen-age style known as "ponytail" or "horsetail".

A few of the fairly uniform case histories will be reported below.

CASE REPORTS.

Case 1.—A girl aged 10, who for the past year had been doing her hair in a tight "ponytail". During the past month her parents had been alarmed at noticing the development of nearly bald patches on both sides of her neck.

Examination revealed conspicuous thinning of the hair on the neck, but also at the temples, i.e. the regions where the traction was most pronounced. Closer inspection of these areas showed groups of inflamed follicles, some of which were infiltrated and covered by a small scale, while others were marked only by perifollicular erythema.

She was advised to change to a looser hair style, and no other treatment was given. Two months later, the signs of inflammation had subsided and a vigorous growth of hair had begun.

Case 2.—A girl aged 18, who had been doing her hair in the "ponytail" style for the past year. Three weeks ago, she had noticed thinning of the hair around the transverse parting on the anterior vertex.

Examination showed in the frontal region irregular alopecia with atrophy of numerous hair follicles and diffuse thinning in the marginal zone. In a few of the remaining follicles there were delicate scales.

Her hair style was altered, and two months later hair growth was again vigorous in the marginal zone of the alopecia, whereas the atrophic areas in the centre remained unchanged.

Case 3.—A girl aged 10, who for the past year had been doing her hair in a "ponytail"—which had now almost disappeared owing to severe hair loss.

Examination revealed diffuse thinning of the hair, particularly at the nape of the neck, but also at the temples and on the anterior vertex. There was no follicular atrophy, but many of the follicles were empty.

The patient did not attend for follow-up, but her parents reported one year later that the hair growth had become normal after a change of hair style.

Case 4.—A girl aged 8, who had been doing her hair in a "ponytail" for the past 18 months. During the past year she had suffered increasingly from loss of hair which now made it difficult to do the hair in the accustomed way.

Examination showed thinning of the hair at the neck and temples (Fig. 1). At that time no follicular inflammation or atrophy was observed.

Treatment consisted in a change of hair style. One year later, hair growth was dense at the back, but on both temples there remained a diffuse thinning with follicular atrophy.

COMMENTS.

The modern "ponytail" has a marked resemblance to the traditional Greenlandic top coiffure (Fig. 2). In Greenland, this hair style persisted until a few decades ago, even though it often gave rise to patches of permanent baldness.

This type of alopecia was first described by the Austrian dermatologist Trebitsch (1907 ; 1908). Travelling in West Greenland in the early part of



FIG. 1.

this century, he noted a characteristic baldness amongst the women. It started in the parietal regions in young girls, spreading later to the back of the head and the temples. Trebitsch noticed that the baldness persisted even when the hair style was later changed, but that it never affected women who had done their hair in the European way since childhood. Since traumatic alopecia of this type had not been observed elsewhere, Trebitsch named it "alopecia Groenlandica".

The traditional coiffures of Japanese women were later reported to result in similar patches of baldness, but of different localization according to the national hair style (Aramaki, 1931).

In Europe, marginal alopecias were first noticed by Sabouraud (1931).

In his patients the hair loss was usually on the forehead and caused by gathering a bun at the back of the head, so he named it *alopecie liminaire frontale*. Subsequent authors have chosen the broader term, "traumatic marginal alopecia" (Costa, 1946; Behrman, 1952). At present, the condition is particularly common among American Negro women as a result of too energetic treatment for straightening their frizzy hair (Behrman).



FIG. 2.

CLINICAL FEATURES.

The chief sign of traction alopecia is symmetrical baldness or thinning at the hair line. As a rule, the lesion is localized to the temples, but it may also affect the back of the head, the forehead, or the parting, depending on the hairdressing style. A characteristic finding is a thin straggling strip of hair at the distal margin of the alopecia, where the hairs are preserved because they have been too short to be gathered by the hair fasteners. Closer inspection often reveals patches of follicular atrophy and at times scattered folliculitis or perifollicular erythema. In the incipient stages, the patches of folliculitis may be closely grouped with firmly adherent crusts or scales suggestive of seborrhoeic eczema.

The cause of the hair loss is constant traction on the hair. This may be due,

as in the cases we have seen, to a tightly gathered coiffure, but the use of curlers or hair grips may also contribute. Some of the tightened hairs loosen without local reaction, but in many areas the traction induces an inflammation of the hair follicles. The folliculitis heals once the hair has been shed and the trauma thus removed, but the follicles undergo atrophy and cicatricial alopecia gradually develops. The hair loss is accelerated by the presence of pityriasis.

Treatment simply consists in a change of hairdressing style.

In Greenland, where the top coiffure was preserved throughout life, the alopecia progressed slowly and continuously. The modern equivalent of the Greenland hair style (the "ponytail"), on the other hand, is only used for a few years, usually by very young girls. Only a few develop actual alopecia during this period, but many may exhibit some thinning of the frontal and temporal hair which escapes notice until it has become far advanced. If the hair style is altered early enough, the thinning will regress, but follicular atrophy may occur very early. A change of hair style should therefore be recommended if there is the slightest sign of thinning.

SUMMARY.

In 11 young Danish girls the modern hair style known as "ponytail" induced hair loss of the same type as alopecia Groenlandica (Trebitsch).

The chief signs were hair loss, especially in the temporal regions, scattered patches of folliculitis, and follicular atrophy. Changing the hair style usually resulted in renewed growth of hair, but in several cases the thinning was permanent.

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ROYAL SOCIETY OF MEDICINE

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President—Dr. LOUIS FORMAN.

15 November 1956.

Recurrent Non-scarring Granuloma of the Face.—Dr. C. H. WHITTLE and Dr. A. J. ROOK.

A woman, aged 37.

The patient began to get "blind boils" on the chin in 1952. At the first attendance (12.xi.52) she presented a tender, discoid, plum-coloured swelling of the left cheek, 4 cm. in diameter and of granulomatous consistency, which had been present for three weeks, starting as one of these "boils". She was shown here on 15.i.53 (Beck and Whittle, 1953) and several members thought the lesion was a kerion. It slowly increased in size to a diameter of 12 cm., became painful and showed crusting and oozing.

Full investigations, as recorded in the published account, yielded no clue to the nature of the lesion. Subsequent repeated bacterial and mycological investigations have also proved negative.

In March 1953, after 4 months in which all treatment had failed, she was given aureomycin 500 mg. six-hourly by mouth. The dose was halved after 4 days and again halved 11 days later. After the first few days, the lesion lost its angry character, started to dwindle and eventually faded, leaving no trace except slight pigmentation.

The first recurrence took place in June 1953, since when there have been repeated relapses. In each relapse, the administration of aureomycin by mouth for 7 days has been followed by resolution, which has started about 5 days after commencing the treatment. Lesions have appeared on the other cheek and on the chin, but at no other sites. In no attack has there been any constitutional disturbance.

Blister fluid grew no significant organisms and virus studies for herpes simplex were negative. Drugs have been excluded as a cause, and on 11.vii.56, when the lesions were active, the blood contained no bromide (i.e., by Conway's method, less than 0.04 mg. per 100 ml.).

Histology (15.xii.52) (A. M. Barrett).—Intense granulomatous inflammatory reaction with eosinophils and predominantly neutrophils, extending deep into corium, perivascular, and sparing the papillary layer. Gram, periodic-Schiff and toluidine blue staining showed no micro-organisms.

Comment.—This case is shown for its curious features viz., (i) absence of any demonstrable infective or chemical agent, (ii) recurrence over several years, limited to the face, (iii) "boils" or herpetiform pustules in the early stage of the lesions, (iv) complete resolution without scarring and (v) apparent response to aureomycin.

Robert (1939) reported a case which he regarded, without any proof, as a granulomatous form of herpes simplex, but there were no recurrences and his illustrations of the lesions and their histology suggest a verrucous rather than a granulomatous nature.

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DISCUSSION.

Dr. W. N. GOLDSMITH : We have had a patient, regarded as a case of infective granuloma, who strenuously denied taking any drugs, but nevertheless has a very high blood bromide figure.

Dr. H. HABER : The infiltration is surrounding blood vessels and the picture resembles an allergic vasculitis. Could it be an allergic granuloma ?

Dr. I. B. SNEDDON : The early lesion suggests the deep papular type of erythema annulare centrifugum described by Darier. I have seen two or three cases of that condition which have lasted many months.

Dr. C. H. WHITTLE : Though Dr. Haber's remarks are very interesting the effect of the aureomycin is not in my opinion antibiotic. It is akin to the occasional remissions we used to obtain in cases of pemphigus or pemphigoid following not only the giving of aureomycin (Bettley, F. R., 1950, *Lancet*, i, 66), but also of such drugs as antrypol, which as far as I know has no antibiotic properties. The mode of action is obscure, but it may possibly be *via* the endocrines.

Dr. F. RAY BETTLEY : I should like to say with regard to Dr. Whittle's remarks that about three years ago I gave aureomycin to a patient with the dystrophic form of epidermolysis bullosa. I gave him a week's treatment with aureomycin and he himself assured me he had no doubt whatsoever that his susceptibility to trauma had been considerably altered by this. He also got unpleasant abdominal symptoms and almost constant diarrhoea, but he was quite sure that the occurrence of blisters was partly prevented.

Dr. W. N. GOLDSMITH : An experiment was carried out by A. Jarrett which showed that the separation of the dermis from the epidermis by trypsin was inhibited by aureomycin. It appears to have an anti-enzyme action.

Dr. F. RAY BETTLEY : I attempted to determine the effect of aureomycin on cantharides blisters. After one week's treatment with aureomycin (2 gm. daily) the production of cantharides blisters was apparently unaltered.

Dermatitis Herpetiformis.—Dr. W. FRAIN-BELL (for Dr. R. T. BRAIN).

A girl, aged 4½.

History.—Blisters first appeared on the vulva in January 1956 and the reaction remained confined to this area during the first few months, except for an occasional lesion on the thigh. When first seen in March 1956, one or two small bullae were present on the thighs. The main reaction was confined to the vulva, presenting as active bullae and pustules at the periphery with central scaling. The process gradually spread from the surface of the labia out on to the pubic area (Fig. 1). There was minimal irritation. No other abnormalities were detected and her general health was otherwise good. Repeated examination of the blood was normal except for 3% eosinophilia on one occasion.

Histology.—A sub-epidermal bulla is present. The overlying epithelium shows minimal balloon degeneration. The bulla contains lymphocytes and polymorphs and a moderate number of eosinophils. The underlying dermis and the adjacent dermal papillae contain considerable numbers of lymphocytes and polymorphs and there is a perivascular round-cell infiltration in the deeper dermis (Fig. 2).

Treatment and progress.—Complete remission within 7 to 10 days followed the administration of diamino-diphenylsulphone (dapsone) on 3 occasions, requiring however a dose of 50 mg. a day; reasonable partial remission was maintained with a dose of 150 mg. a week. A short course of prednisone (155 mg. in 10 days) produced no benefit. Moderately severe anaemia resulted from the administration of dapsone and it was not possible, despite additional iron by mouth, to maintain a level of haemoglobin above 70%, even with the small dose of 150 mg. weekly. During an observation period of 9 months, occasional spread has taken place to the buttocks and thighs with a few bullae on the arms, the main lesions, however, being confined to the vulva.

Comment.—Although the genitalia are commonly affected in dermatitis herpetiformis in children, this case was unusual in so far as the bullous eruption remained



FIG. 1.

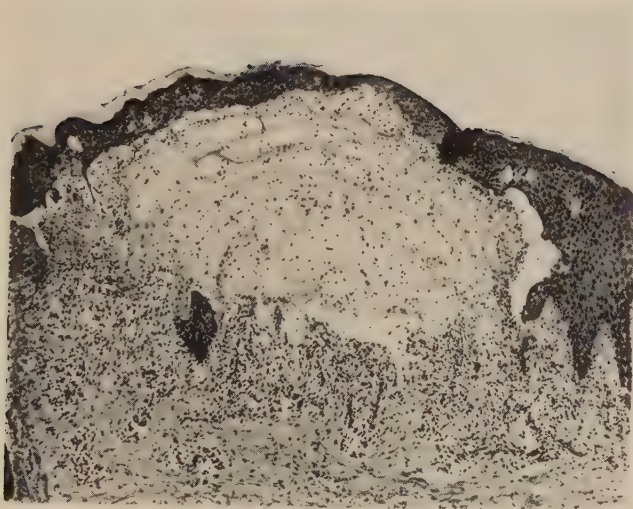


FIG. 2.

virtually confined to the vulva for many months at the start, and at all times has been most severe in this area.

Postscript.—January 1957: She is now very much improved. Constant formation of bullae is still occurring on the vulva and to a less extent on the upper thighs, but the lesions in all affected areas are much less numerous. The haemoglobin is now 84% and the dose of dapsone has been reduced to 100 mg. a week.

DISCUSSION.

Dr. H. R. VICKERS: I am very pleased our Scottish colleagues are here because at the Edinburgh meeting it was quite evident that the farther north one goes the more common these cases are. We in Sheffield are half-way to Scotland and we see a number of these cases. Our experience has been that they grow out of this condition at about puberty. Some of these children require quite high doses of dapsone. I have a girl who has had 75 mg. daily for 3 years, and no dosage below that effectively controls her condition. Her haemoglobin never goes above 70%, but she seems quite well.

Dr. G. A. G. PETERKIN: On going over the old cases treated by the late Dr. Fred Gardiner, I found one had persisted and all the other had cleared completely before puberty. Dr. Gardiner used arsenic in quite large doses and it seems to have had no bad after-effects.

Dr. J. FERGUSON SMITH: I can confirm the higher frequency of these cases in the north. In 1922, at the B.M.A. meeting in Glasgow, I showed a number of cases; in the 'thirties I had 9 of these juvenile cases under observation. We did a follow-up shortly before the war and found that only one had failed to clear up of all those we traced. That was where a brother and sister were both affected and the sister had not recovered when I last saw her in her twenties. In those days arsenic was our only effective remedy.

Dr. I. S. HODGSON-JONES: I have a case at the moment, a child of 2 years, who gets acute haemolysis on the very smallest doses of dapsone. In desperation we have been trying prednisolone 5 mg. three times a day. This seems to be controlling it. I wonder whether anyone has experience of this drug in this condition?

Dr. W. N. GOLDSMITH: On the toxicity of dapsone, I should like to ask whether anyone has experience of Promacetin, a Parke Davis product, which is not available here.

Dr. A. SCOTT, a visitor: We reported 12 cases treated with Promacetin in New York the results of which were very good, and the reason for its use is that the toxicity is much lower. In fact there was no real toxicity in those 12 cases. It is used in preference to dapsone in America now.

Norwegian Scabies.—Dr. I. MARTIN-SCOTT.

History.—Early in June 1956, this unmarried lorry driver of 35 presented himself at hospital complaining of a warty and irritant eruption of one year's duration.

Examination.—The patient was of slight build and average intelligence. On the knees, elbows and buttocks there were discrete psoriasiform plaques. On the extensor aspect of the fingers and toes (Figs. 1 and 2) and on the wrists and ankles there were warty ridges surrounded by a violet halo. A tentative diagnosis of psoriasis, hypertrophic lichen planus or a syphilide was made, and a biopsy performed on the hand. This showed galleries of mites in the keratin layer.

Two months later I developed vesicles beneath my watch buckle when on a seaside holiday. Thinking perhaps the salt water had induced a nickel sensitivity, I changed the watch to the right wrist but no eczema developed. On return home, a 2% nickel sulphate patch test was negative.

Three months after I had seen the case my wife developed generalized irritation, and the diagnosis of my localized eczema of wrist without any burrows was embarrassingly obvious. Thirty slides of scrapings from my wrist were examined before a single acarid was discovered.

The usual incubation period for scabies in first infections is two to four weeks, but in my own case it was eight weeks.

The management of this case was greatly handicapped by the patient's irregular attendances at hospital. Since this is a very contagious type of scabies I feel it should



FIG. 1.

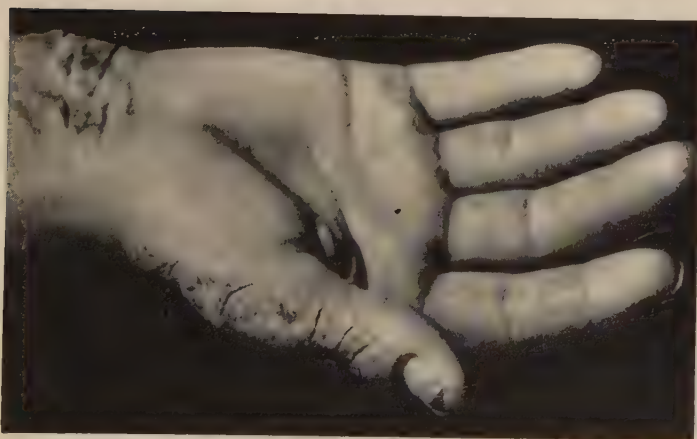


FIG. 2.

be notifiable, so that health authorities could enforce the isolation of such cases until the completion of treatment. In this present case the patient drove his lorry all over England and no doubt over the year infected many persons by chance contact. (This patient did not attend the meeting, but colour photographs were shown.)

Ectopic Cutaneous Schistosomiasis. Dr. H. HABER and Dr. J. G. COWLEY.
H. L—, student aged 22, native of Accra, Gold Coast.

History.—She has bathed in rivers in an endemic area of bilharziasis and noticed that her skin was itchy after leaving the water. In 1948, she noticed blood in her urine and bilharziasis was diagnosed, for which she received 40 intramuscular injections. In June 1956, she noticed the sudden appearance of slightly itchy papules on her upper abdomen, right supra-clavicular fossa, and below the right clavicle. During the past 4 months the papules have subsided, leaving hyperpigmented macules.

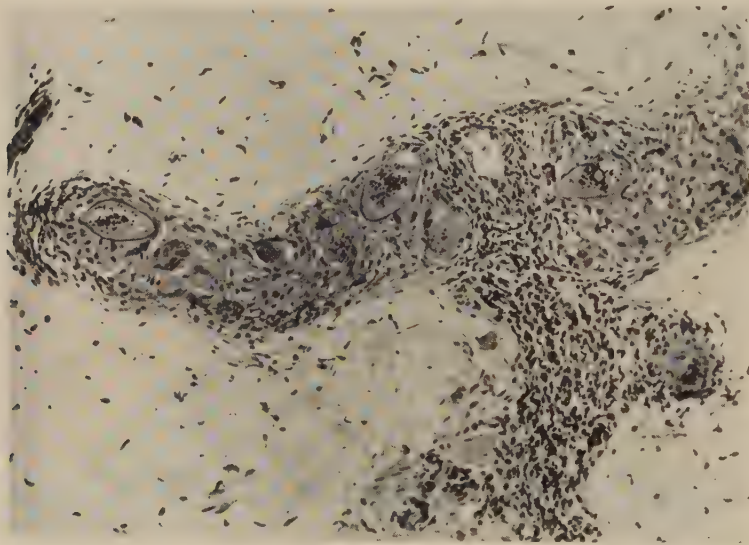


FIG. 1.

Investigations.—Two 24-hour specimens of urine revealed neither red blood corpuscles nor ova. Blood count normal, no eosinophilia.

Skin biopsy showed terminally spined ova morphologically indistinguishable from *Schistosoma haematobium* (Fig. 1).

O. D. STANDEN, D.Sc. : The condition of the schistosome eggs as seen in sections of skin taken at biopsy indicates that this girl is still infected and has only partly responded to the treatment given 8 years ago. She assured me that she had not been exposed to infection since that time. Since the eggs contain miracidia and show no marked signs of degeneration, it may be assumed that they are of quite recent origin. The problem arises as to how such viable eggs might find their way to ectopic sites in the subclavicular and abdominal regions. Obviously, a great deal of speculation is involved but it is worth considering the possibilities in the light of our knowledge of the life cycle of *Schistosoma haematobium* and the mode of drug action upon schistosomes generally.

Consideration should be given first to the possibility of viable eggs finding their way to these sites when the adult paired worms are sited in their normal position in

the vesical venules or venules of other organs in the pelvis. We know that although large numbers of eggs pass through the wall of the bladder to be excreted with the urine, many are swept back with the blood stream and tend to accumulate in the lungs and the liver. It is conceivable that occasionally eggs may pass from the venous capillaries of the lung to the arterial capillaries and so enter the systemic circulation, but this is improbable. Further, the possibility of *groups* of eggs reaching the same peripheral site is remote. It therefore seems very unlikely that the eggs found in these ectopic lesions were produced by schistosomes living in the venous system of the pelvis.

There is then the probability of the lesions being due to egg-laying by schistosomes living ectopically. It must be remembered that the schistosomes are unisexual and that the presence of viable eggs indicates the presence of paired worms and not single specimens. It is known that following infection, schistosome cercariae penetrate the lymphatic capillaries, traverse the lymph nodes, enter the blood stream by way of the main lymphatic ducts and take up their position as adults in the venous system. With *S. haematobium* it is the urogenital system that is usually involved. Theoretically, the following possibilities arise:

(i) Cercariae may penetrate no further than the immediate area of exposure to infection and develop to adults ectopically.

(ii) Cercariae distributed in the systemic circulation in the post-pulmonary stage may develop ectopically.

(iii) Adult paired worms, disturbed by inadequate drug treatment, may migrate to ectopic positions.

It is considered that (i) is most improbable and that there is no evidence that this could occur. Indeed, there is evidence that cercariae that fail to leave the skin are destroyed by phagocytes in the course of a few days; (ii) may also be dismissed on grounds of improbability. This solution would demand not only ectopic survival and development but also the coincidental distribution of at least one male and one female cercaria at each of the two sites where lesions are manifest. Possibly (iii) offers the most logical though speculative answer. It is known that following the treatment of experimental infection with *S. mansoni* in mice, the affected worms are removed from their normal position in the mesenteric veins and are swept passively with the blood stream to the liver. Here they may die or, if inadequately treated, recover and remigrate up the mesenteric veins, recommence egg-laying and provide a picture of clinical relapse. It seems reasonable to assume that something similar occurs with this species in man. With *S. haematobium* it is not possible to reproduce a urogenital infection in small experimental animals and a direct comparison cannot therefore be made. However, it is perhaps reasonable to assume that something similar occurs with *S. haematobium* in its reaction to drug treatment. If so, this provides a possibility that those pairs of worms not caught up in the venous anastomoses of the urogenital system may get swept forward into the inferior vena cava. If at some point in this journey they recover from the effects of the drug and resume their normal tropistic tendency to migrate against the direction of the flow of blood, it is conceivable that they may wander, as pairs, into some ectopic position and then, for a time, recommence the production of eggs.

These arguments are necessarily speculative, but in the light of our knowledge of the life cycle of schistosomes and their response to drug action, it would seem that ectopic migration of paired worms following inadequate treatment offers a possible explanation for this apparently rare condition.

Ichthyosiform Erythroderma (Brocq).—Dr. H. WILSON and Dr. H. HABER.

A woman, aged 36.

History.—The second day after birth, a crop of blisters developed on this patient's skin. During early infancy, further crops appeared and there was widespread scaling.

In September 1921 she was treated with $\frac{1}{3}$ pastille dose of x-rays which caused temporary remission. In April 1922, she was readmitted having developed tylosis of hands and feet and marked hyperkeratosis over the elbows, knees and neck. The following month she was presented at the Dermatological Section of the Royal Society of Medicine (O'Donovan, 1922).

Past history.—Pneumonia in infancy—no other serious disease.

Family history.—Father died of aortic aneurysm, mother alive, suffers from angina, one brother alive and well. No family history of skin disease.

On examination.—She is well built, intelligent and co-operative.

There is hyperkeratosis of the forehead, nasolabial folds and chin. More exuberant hyperkeratosis affects the sides of the neck, the axillary folds, the elbow flexures and the popliteal spaces. On the extensor surfaces of the arms and legs the hyperkeratosis tends to be linear, and on the trunk it is occasionally follicular. There is gross hyperkeratosis of the palms and soles and active and healed blisters on the dorsal surfaces and sides of the hands and feet. There is no abnormality of the teeth, hair or nails and the internal organs appear normal.

Blood count.—Normal.

REFERENCE.

O'DONOVAN, W. J. (1922) *Proc. roy. Soc. Med.*, **15**, *Sect. Derm.*, 49.

Histology (Dr. H. Haber).—The epidermis shows very marked solid hyperkeratosis in some places, and in others this is of the basket-weave type. There are a few patches of parakeratosis. The characteristic changes take place within the stratum granulosum and spinulosum. Within the stratum spinulosum one can observe disintegration of the rete by acantholysis as seen in "Hailey-Hailey disease". This change continues well into the granular layer, where in addition to acantholysis one can also see severe changes within individual cells. This leads to reticular degeneration of the whole area, amounting to intra-epidermal vesicle formation. The changes within the corium are negligible (Fig. 1).

The histology, therefore, is very characteristic and amply explains the mechanism of bulla formation. It is not due to superimposed impetigo or excessive sweating, nor is it a combination with epidermolysis bullosa.

Dr. HABER: I recently saw a case in a boy aged 13 years who developed in the first month of life typical systematized ichthyosis hystrix, the histology of which was the same as the case we have seen to-day. This fact indicates that ichthyosis hystrix showing the typical histology may be a variant of ichthyosiform erythroderma.

On the other hand there are cases diagnosed clinically as ichthyosis hystrix which show the histology of verrucous naevi. A case was shown to me by Dr. Robert Cairns in a girl aged 18 years who had typical ichthyosis hystrix. The histology (Haber, 1955) revealed irregular verrucosity of the epidermis, sebaceous glands, apocrines, organoid basal cell epithelioma and syringocystadenoma papilliferum, a picture which one usually finds in the so-called sebaceous naevus of Jadassohn. This goes to show that ichthyosis hystrix can be of two types, the first a variant of ichthyosiform erythroderma and the second an epidermal verrucous naevus.

In 1897, Nikolsky presented to the Third International Congress of Dermatology a case of acanthokeratolysis universalis congenitalis which might have been a case of bullous ichthyosiform erythroderma. J. G. Reyes (1945) published a case of epidermodysplasia hystrioides bullosa. Judging from the clinical picture and the histology, his case was identical with ours. Barker and Sachs (1953) were the first to point out that bullous ichthyosiform erythroderma was a variant of the non-bullous type and that ichthyosis hystrix was a variant of bullous ichthyosiform erythroderma. I would like to add that only some cases are variants of ichthyosiform erythroderma; some are verrucous naevi.

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 NIKOLSKY, P. in *Comptes Rendus du XII ième Congrès International de Médecine, Moscow, 1897, Section 8, Dermatologie et Vénériologie*, p. 437.
 REYES, J. G. (1945) *Arch. Derm. Syph., Chicago*, **52**, 328.

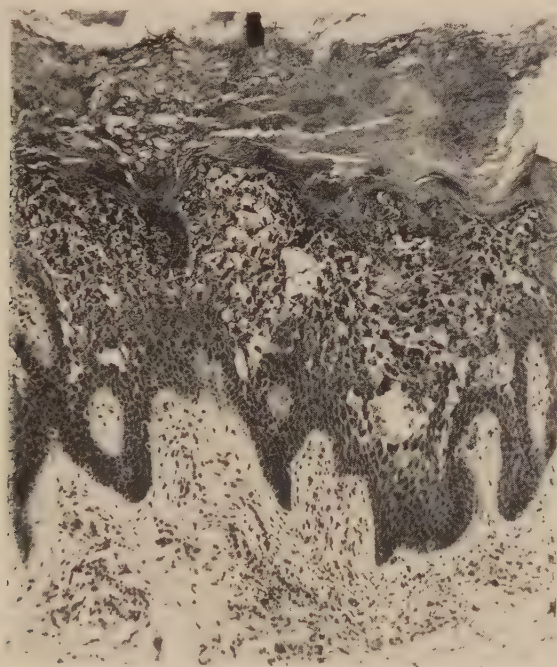


FIG. 1.

The following cases have been published in *Proc. roy. Soc. Med.*, **50**, 275.

Tuberculous Glands with Skin Involvement.—Dr. S. P. HALL-SMITH and Dr. J. McMURRAY.

Acanthosis Nigricans.—Dr. P. J. HARE.

Necrobiosis Lipoidica.—Dr. P. J. HARE.

The following cases also were shown :

Chronic Oedema of Hand.—Dr. W. D. FLETCHER and Dr. A. JARRETT.

Tuberculoid Leprosy.—Dr. W. H. JOPLING (for Sir GEORGE MCROBERT).

Keratoacanthoma of the Lower Lip (Red Margin).—Dr. C. H. WHITTLE and Dr. R. A. DAVIS.

Pemphigoid.—Dr. M. WITHAM (for Dr. W. N. GOLDSMITH).

Familial Macular Pigmentation and Nerve Deafness in (a) Mother and Child and (b) Unrelated Male.—Dr. I. MARTIN-SCOTT.

Disseminated Granuloma Annulare.—Dr. PETER SMITH.

NORTH OF ENGLAND DERMATOLOGICAL SOCIETY.

March 1957.

Herpes Gestationis.—Dr. I. B. SNEDDON.*Case 1.*—A woman aged 32.

This patient was first seen when she was 5 months pregnant. She had then had an intensely irritable erythematous and bullous eruption for 2 months and was becoming distressed from lack of sleep. Antihistamines had been tried with no benefit.

Previous obstetric history.—First child, a girl, born in 1948. Second child, a boy, born in 1953. Three days after his birth she developed an intensely irritable erythema multiforme-like eruption which lasted a month and was diagnosed as puerperal herpes gestationis.

Examination.—Extensive bullous eruption on trunk and limbs. The bullae arose from erythematous annular lesions. Blood pressure 120/55.

Investigations.—E.S.R., Wintrobe 24. Hb 77%. W.B.C. 12,000, with 12% eosinophils.

Urine normal. Gonadotropins, 17-ketosteroids and ketogenic steroids—normal values.

Histology (7.iii.57).—There is a subepidermal vesicle. Eosinophils are present in the vesicle and in the adjacent dermis. The appearances are consistent with dermatitis herpetiformis.

Progress and treatment.—There was no response to sulphapyridine and correction of her iron deficiency anaemia, but prednisolone 5 mg. *t.d.s.* produced immediate lessening of the irritation and considerable but incomplete clearing of the eruption.

She was maintained on the same dose until she was delivered of a male infant on 3.iii.57. Prednisolone was discontinued after she went into labour but had to be started again 3 days later as the eruption relapsed severely.

Prednisolone was again withdrawn 4 weeks after delivery and the patient's skin remained well.

Case 2.—A woman aged 41.

This patient was seen when 5½ months pregnant. Sixteen days previously she had developed a widespread itching and blistered eruption.

Previous obstetric history.—Daughter aged 9. Daughter aged 7. Miscarriage 5 years ago. Son born in 1954, who died of whooping cough aged 16 weeks. During the last 4 months of that pregnancy she suffered from a generalized itching rash which cleared 3 weeks after parturition.

Examination.—Erythema multiforme-like lesions on the thighs, legs, forearms and shoulders. On the inner aspect of the forearms numerous small bullae were present: Confluent erythema of the thighs and oedema of the legs. B.P. 110/70.

Investigations.—W.B.C. 16,000; eosinophils 10%. Urinary gonadotropins, ketosteroids and ketogenic steroids normal.

Progress and treatment.—There was no relief from antihistamines but the eruption and itching were controlled with prednisolone 10 mg. *b.d.* Cortisone 25 mg. *t.d.s.* was substituted because she developed intense heartburn while on prednisolone.

Postscript.—She was delivered of a live normal child.

Relapsing Panniculitis.—Dr. P. D. C. KINMONT.

A married woman of 40 was first seen on 19.iv.56. She had a 2-year history of large painful lumps appearing in the subcutaneous tissue of the limbs and trunk. The appearance of a new lesion was accompanied by malaise and sometimes by swelling of the knees and ankles. Sulphapyridine had been tried without effect during the first year.

Past history.—Occasional sore throats.

Family history.—Nil relevant.

On examination.—She has a smooth red plaque in the subcutaneous tissue of one thigh and a yellow nodular plaque on the left shoulder. There are also atrophic pigmented scars with central depressions scattered over the body.

Histology (28.iv.56).—There is subcutaneous fat necrosis with a foreign body giant cell reaction. The appearances are those of Weber-Christian Disease.

Progress.—She was seen again on 31.xii.56, when she had a severe relapse which followed a sore throat. During January 1957 she felt ill and developed several nodules on the thighs and an indurated plaque in the left antecubital fossa. More nodules developed on the site of bruises on the thighs.

She was given prednisone 20 mg. daily on 8.i.57 and was admitted to hospital on 19.i.57.

She was then apyrexial but had many red or purple plaques scattered over the body. Some were discharging a yellow material.

Investigations.—E.S.R. 20 mm. in 1 hour. Blood count normal. Serum cholesterol 132 mg.%. Serum proteins 5.8 g.%. Normal A/G ratio ; slight increase in gamma globulin. Blood urea normal.

Swab from a lesion showed scanty debris and *Staphylococcus aureus* was cultured.

Urine normal. Skiagram showed an infected maxillary antrum.

Prednisone was increased to 40 mg. daily with no benefit. After a course of penicillin and antral washouts she improved and since February 1957 she has had no new lesions.

BOOK REVIEW

PRACTICAL DERMATOLOGY.*

THIS small, but not inexpensive, book of some 370 pages is designed as a handbook for the busy general practitioner and the authors emphasize that the views contained therein are purely personal.

After a concise and practical introduction to diagnosis and treatment there is given a short discussion of most classes of cutaneous disorders, but it is doubtful if the aim of describing "the dermatologic disorders as they are met with in daily practice" is achieved by giving almost equal prominence to the bullous dermatoses and the collagen diseases as to the eczema group, and by including subjects such as amyloidosis cutis.

As the book is written primarily for the practitioner in the U.S.A. a working knowledge of the drugs in common use there is an advantage, particularly as many proprietary preparations are mentioned, some of which are not imported to Great Britain and for which no British equivalent is available. A very sensible attitude is maintained to the use of corticosteroids, with a full realization of the cost factor. In discussing the therapy of various disorders, however, the personal practical methods have been largely omitted to make room for the naming in general terms of types of drugs found useful. The few prescriptions given for local applications would be accepted generally as orthodox. The Hotchkiss-McManus stain is mentioned for direct examination of specimens for fungi, but surely the busy practitioner might save a little time by trying caustic potash or caustic soda first.

There is an annoying number of minor contradictions and in a few places the meaning of a sentence is not very clear; these are carping criticisms of a book which will no doubt prove useful to many a practitioner, but, in the opinion of the reviewer, rather in the United States than in Great Britain.

The illustrations vary from excellent to rather poorer than one is accustomed to look for in an American text-book.

T.E.A.

**Practical Dermatology*. S. M. PECK and L. L. PALITZ (1957). New York: Landsberger Medical Books, Inc. Pp. 380. Illus. 122. Price 52s. 6d.

CURRENT LITERATURE

THE PENETRATION AND DISTRIBUTION OF C^{14} HYDROCORTISONE IN HUMAN SKIN AFTER ITS TOPICAL APPLICATION. A SCOTT and F. KALZ. (1956) *J. invest. Derm.*, 26, 149.

Although the physical half life of C^{14} is 5000 years it has been found that the biological half life is only 12-18 days and that there is no tendency for the element to persist longer in some tissues than in others. This has removed the objection to using C^{14} as a tracer: so here is an autoradiograph study of ointment penetration.

The experiment shows that hydrocortisone is evenly absorbed through all parts of the epidermis, and that after 6 hours it is, or at any rate its C^{14} atoms are, concentrated round the blood vessels; and in 16 hours they are gone. The vehicle makes little difference but U.V.R. erythema accelerates penetration.

J. H. T. D.

OBSERVATIONS ON THE ORIENTATION OF KERATIN IN THICKENED CORNIFIED EPITHELIUM OF THE HUMAN SKIN. A. G. MATOLTSY and G. F. ODLAND. (1956) *J. invest. Derm.*, 26, 121.

Hair, nails and horny layer are all constructed of the same alpha-keratin molecules but the arrangement differs. In hair the long axes are parallel to the shaft, in nail "perpendicular to the long axis" (at right angles to the plate or parallel to the surface) and in the horny layer of the sole parallel to the grooves, crossing the ridges and encircling the sweat pores.

J. H. T. D.

A COMPARISON OF THE INHIBITORY EFFECT OF A 9 α FLUOR-HYDROCORTISONE ACETATE AND HYDROCORTISONE ACETATE OINTMENTS ON ECZEMATOUS REACTIONS PRODUCED BY ELECTROPHORESIS OF ALLERGENS. H. HANSTHAUSEN. (1956) *J. invest. Derm.*, 26, 111.

9 α fluor-hydrocortisone is much the better but the effect is not constant and is rarely complete.

J. H. T. D.

THE IN VITRO METABOLISM OF TESTOSTERONE BY HUMAN SKIN. H. H. WOTIZ, H. MESCON, H. DOEPFEL, H. M. LEMON. (1956) *J. invest. Derm.*, 26, 113.

The metabolism is estimated by comparison of the quantity of testosterone with that of desoxy-pentose nucleic acid remaining in the tissue after 3 hours aerobic incubation in an apparatus somewhat similar to the Warburg manometer. It was already known that healthy skin and mammary gland metabolized actively and breast carcinoma nearly 5 times as actively as skin. This experiment shows that scalp is about twice as active as axilla or back.

J. H. T. D.

THE EFFECT OF CHLOROQUINE PHOSPHATE IN MODIFYING REACTIONS TO ULTRA-VIOLET LIGHT. M. M. CAHN, E. J. LEVY and B. SHAFFER. (1956) *J. invest. Derm.*, 26, 201.

It seems impossible that the skin can receive any direct protection by chloroquine because the main absorption spectrum is between $\text{\AA}$ 3200 and $\text{\AA}$ 3400, and quite minimal below $\text{\AA}$ 3100 where lie the action spectra for erythema and the papular reaction of polymorphous light eruption.

The authors claim to have succeeded in obtaining a distinctive papular reaction in 11 of their 21 patients by means of hot quartz light and in showing that it is inhibited by 4 weeks' treatment with chloroquine at the same time proved to be ineffective against reactions to sunburn, histamine, trichophylin and poison-ivy antigen.

The success of chloroquine in the treatment of polymorphous light eruption, lupus erythematosus, and indeed in rheumatoid arthritis remains obscure.

J. H. T. D.

A MICROANATOMICAL STUDY OF THE RESPONSE OF THE PILOSEBACEOUS APPARATUS OF THE RABBIT'S EAR CANAL. G. M. HAMBRICK and H. BLANK. (1956) *J. invest. Derm.*, 26, 185.

A minor plastic operation exposes a convenient field of the specialized skin of the rabbit's external auditory meatus. Here in contrast with the grouped hairs and diminutive sebaceous

glands of the furry skin we have a dense mass of sebaceous glands each with a single hair. Plucking initiates a regular hair cycle but this is not accompanied by obvious changes in the sebaceous gland.

Testosterone increased the sebaceous gland volume of spayed females by about 60% but progesterone and 17 hydroxyprogesterone not at all.

Halowax not only brings about epithelial hyperplasia and follicular plugging but damages the gland. It does not interfere with hair growth nor does it cause horny cyst formation.

J. H. T. D.

FAT IN THE SKIN OF THE MOUSE DURING CYCLES OF HAIR GROWTH. G. N. BORODACH and W. MONTAGNA. (1956) *J. invest. Derm.*, **26**, 229.

There is no real increase in the amount of fat contained in the panniculus though it may appear in this section to be much thicker during the later phases of anagen.

J. H. T. D.

IN VITRO ACTIVITY OF *p*-HYDROXYBENZOIC ACID ESTERS ON PATHOGENIC FUNGI. F. C. BOCOBO, C. MOPPER, E. R. HARRELL and A. C. CURTIS. (1956) *J. invest. Derm.*, **26**, 239.

These esters (of an acid isomeric with salicylic) are ordinarily used as preservatives. They are also effective against many pathogenic fungi and will diffuse into a seeded plate out of a blob of ointment.

J. H. T. D.

THE EFFECT OF THE VIBRA-PUNCTURE INTO AREAS OF VITILIGO. D. GRINSPAN, R. CALANDRA and J. FAIRMAN. (1956) *J. invest. Derm.*, **26**, 243.

Of the first 46 patients treated with a tattooing machine, 22 are described as having been cured. The best clinical responses were obtained on the face; fingers and toes were usually difficult. Repigmentation is usually noticed between the 15th and 20th treatment. In some cases repigmentation occurred spontaneously in untreated areas.

Of the next 61, 35 have stopped coming for treatment but 26 are still attending.

EXPERIMENTAL ECTHYMA CONTAGIOSUM (ORF). C. E. WHEELER, M. POTTER and E. P. CAWLEY. (1956) *J. invest. Derm.*, **26**, 275.

Deals mainly with experimental aspects of the disease in sheep; mentions negative results of inoculation in mouse, guinea-pig, chorioallantois, and conjunctiva of rabbit, and the inconspicuous specific lesion obtainable with some difficulty in the skin of the rabbit.

J. H. T. D.

RESPONSE OF THE HUMAN ECCRINE SWEAT DUCT TO DERMAL INJURY. W. C. LOBITZ, J. B. HOLYOKE and D. BROPHY. (1956) *J. invest. Derm.*, **26**, 247.

In order to divide the sweat ducts in mid-dermis incisions were made parallel to the surface: enough of them to yield biopsy samples at a comprehensive series of intervals between 8 hours and 18 weeks. Regenerative activity at both cut ends presented characteristically spiralling formations but it also exhibited the capacity of sweat duct to generate prickle cells.

J. H. T. D.

HISTOCHEMICAL STUDY OF A CASE OF LIPOID PROTEINOSIS. M. G. WOOD, F. URBACH and H. BEERMAN. (1956) *J. invest. Derm.*, **26**, 263.

With description of case, clinical and histological photographs, and a survey of literature having special reference to histochemistry.

J. H. T. D.

A HISTOCHEMICAL AUTORADIOGRAPHIC METHOD FOR DEMONSTRATION OF TYROSINASE IN HUMAN MELANOCYTES NEVI AND MALIGNANT MELANOMA. T. B. FITZPATRICK and A. KUKITA. (1956) *J. invest. Derm.*, **26**, 173.

In order to determine the activity rather than the mere presence of tyrosinase in melanocytes the specimen is incubated for 24 hours with C¹⁴ tyrosine which is then thoroughly washed out leaving the newly-formed C¹⁴ melanin to indicate its presence on a suitable photographic emulsion. It is this activity (which can survive at least a month in deep freeze) of the tyrosinase system that distinguishes the melanocytes of melanoma and blue naevus from those of the hair matrix and simple pigmented moles.

J. H. T. D.

THE GROWTH OF COCCIDIOIDES IMMITIS IN THE GRANULOMA POUCH OF THE RAT WITH THE DEVELOPMENT OF HYPHAE AND OTHER FORMS. E. T. WRIGHT, V. D. NEWCOMER and T. H. STERNBERG. (1956) *J. invest. Derm.*, 26, 217.

Coccidioides immitis, though it forms filaments in artificial media, is supposed always to occur in the lesion "in a characteristic spherule form"; and when filaments have been discovered, for instance in a pulmonary cavity, they have usually been taken for contaminants.

In this experiment both spheroidal and filamentous forms were introduced into cavities within the subcutaneous areolar tissue of rats prepared either by simply inflating with air ("pneoderma") or by following this procedure with a fill of 1% croton oil in order to line the cavity with granulation tissue. Both kinds of cavity were also treated with cortisone.

The findings have removed any doubt that the organism can assume either form for the purpose of earning its living. Conjugation and budding were not however clearly observed. J. H. T. D.

IMMUNOLOGICAL STUDIES IN THE LYMPHOBLASTOMAS. II. THE ABILITY TO DEVELOP AN ECZEMATOUS SENSITIZATION TO A SIMPLE CHEMICAL AND THE ABILITY TO ACCEPT PASSIVE TRANSFER ANTIBODY. A. ROSTENBERG, H. C. McCRAVEY and S. M. GOLDFARB. (1956) *J. invest. Derm.*, 26, 209.

This is not a conclusive nor even a very satisfactory observation; but at least it contributes evidence to support the hypothesis that the skin of patients suffering from diseases of the lymphoma-leukaemia group, though it will react to histamine and give a positive Prausnitz Kustner, is not readily sensitized to allergens. Only 1 out of this series of 31 patients became allergic when 2:4 dinitrochlorobenzene was applied to the skin according to a technique yielding 15% to 50% of successes in normal subjects: and he was a young man not much inconvenienced by the chronic myeloid leukaemia for which he was receiving treatment. The control series however, though it consisted of seriously ill patients having diseases other than leukaemia, is neither sufficiently large nor varied enough satisfactorily to demonstrate that it is not mere cachexia as opposed to defective lymphocytes that is responsible.

J. H. T. D.

PAPER ELECTROPHORESIS OF SERUM PROTEINS IN SELECTED DERMATOSES. M. FELDAKER, L. A. BRUNSTING and B. F. MCKENZIE. (1957) *J. invest. Derm.*, 26, 293.

Contains a description of the technique; a comparison of it with that of Tiselius; and the findings in 69 patients, including 20 with systemic L.E. 7 with dermatomyositis and 6 with pemphigus vulgaris.

J. H. T. D.

A STUDY OF MUSTARD VESICATION. A. J. McADAMS. (1956) *J. invest. Derm.*, 26, 317.

Dichlorethyl sulphide inflicts damage on the skin of experimental animals but it does not readily blister it, even when the surface is moistened with water or saline. When a "vesicle" (presumably he means a small bulla) does result it would appear that selective "necrobiosis" of the basal layer constitutes the mechanism. The absence of sweat glands is here proposed to account for the insignificant elevation (but this can hardly apply to the horse, proverbial for its sweating, which nevertheless likewise reacts to mustard with a mere "doughnut").

J. H. T. D.

PROPERTIES OF HAIR FAT FROM ADULT MALES ACCORDING TO RACE AND HAIR CONDITION. B. K. KROTOSZYNSKI, L. L. GERSHBEIN and S. B. NEEDLEMAN. (1956) *J. invest. Derm.*, 26, 311.

The grease was extracted from hair supplied by the prison barber who had collected separately the clippings from negro and white "full headed" (clearly those who still kept their hair) and "balding" (presumably those who were bald or had begun to go bald). The quantity and composition of the lipoids differ between the races but not between "full headed" and "balding".

J. H. T. D.

HISTOCHEMICAL DISTRIBUTION OF ACID PHOSPHATASE IN NORMAL HUMAN SKIN. G. MORETTI and H. MESCON. (1956) *J. invest. Derm.*, 26, 347.

A comparative study of 3 techniques; full discussion of the importance to the skin of this enzyme; and 43 references to the literature.

J. H. T. D.

TREATMENT OF CHEILITIS EXFOLIATIVA OF THE LOWER LIP WITH HYALURONIDASE. O. RAMIREZ. (1956) *J. invest. Derm.*, 26, 343.

The lesion, which according to the photographs is limited to the red part of the lip, is described as *erythematous*!

J. H. T. D.

THE EFFECT OF THE TOPICAL APPLICATION OF CORTICOTROPHIN HYDROCORTISONE AND FLUOROCORTISONE ON THE PROCESS OF CUTANEOUS INFLAMMATION. A. SCOTT and F. KALZ. (1956) *J. invest. Derm.*, **26**, 361.

In order to inhibit the inflammatory reaction of the skin to U.V.L. 80% mustard oil and 15% HNO_3 , it is necessary to have applied the hydrocortisone, etc. (ACTH seems to be almost as good) not less than 2 hours nor more than 12 hours before applying the irritant. Nothing is gained by increasing the duration of the protective treatment beyond an hour or two. Its use after the irritant has been applied is futile and may even intensify the reaction. It is thought that the steroid inhibits the action of certain materials evolved by the tissues in response to the primary injury.

(It is obvious that hydrocortisone skin foods should be used prophylactically by all who fear that they are likely to suffer from dermatitis.) J. H. T. D.

A STUDY OF HUMAN EPIDERMAL PROTEINS. A. G. MATOLTSY and F. S. M. HERBST. (1956) *J. invest. Derm.*, **26**, 339.

In a previous experiment (*J. invest. Derm.*, **25**, 71) dried and pulverized callosity was studied; in the present one the authors deal with whole epidermis homogenized in the wet state. The same unsatisfying kind of information emerges. J. H. T. D.

A SYNTHETIC DETERGENT AS A PROVOCATIVE AGENT IN PATCH TESTS. S. A. KVORNING and I. B. SVENDSEN. (1957) *J. invest. Derm.*, **26**, 421.

In cases of allergy to nickel and chrome, positive patch tests with weaker solutions of the salt were made possible by the addition of 1% Teepol. Teepol did not however modify the primary irritant effects of 2% bichloride of mercury. J. H. T. D.

THE USE OF DETERGENTS FOR DIRECT MYCOLOGIC EXAMINATION. G. ACHTEN. (1956) *J. invest. Derm.*, **26**, 389.

An aqueous solution of 0.1% Aminol (a cationic detergent) with 0.2% basic fuchsin run under the coverslip and left without heating for 2-10 minutes gives better results than KOH and with less trouble (if one doesn't mind waiting). J. H. T. D.

THE MICROANATOMY OF MILIARIA CRYSTALLINA. G. W. HAMBRICK and H. BLANK. (1946) *J. invest. Derm.*, **26**, 327.

This condition—usually described as a consequence of abnormal cornification or of sudden profuse sweating in the course of fevers—is here studied, in a case of steroid-controlled pemphigus and in a patient in whom the symptom occurred idiopathically, by means both of ordinary sections and of whole mounts. A convincing explanation illustrated by excelled photo-micrographs is offered.

Experiments with the pads of cats demonstrated that the disturbance of desquamation produced by painting with silver nitrate or by protecting from normal friction are both capable of obstructing the delivery of sweat; but neither duct-rupture nor accumulation of Schiff-positive material were observed. J. H. T. D.

FAILURE OF ACTIVE IMMUNIZATION AGAINST TRICHOPHYTON GYPSEUM INFECTION IN GUINEA-PIGS. F. REISS and L. LEONARD. (1956) *J. invest. Derm.*, **26**, 449.

This attempt to immunize was made with a single injection either of commercial trichophytin or of fungus killed by supersonic vibration, with or without the addition to the inoculum of various adjuvants. Although the first two attempts to infect with a recently isolated strain of *T. gypseum* were comparatively unsuccessful all the animals responded to a supposedly virulent strain obtained from another source, with the normal clinical manifestations.

(This is a piece of routine work over which great pains have evidently been taken but of which the significance, if any, could easily escape the reader—for whom there is no attempt to supply basic information.) J. H. T. D.

STUDIES OF HAEMOSTASIS IN THE EHLERS-DANLOS SYNDROME. P. G. FRICH and J. D. KRACHUTC. (1956) *J. invest. Derm.*, **26**, 453.

By a process of exclusion the facile bruising, formation of haematomas and positive Rumpel-Leede test of the Ehlers-Danlos syndrome are all attributed to the collagen defect.

J. H. T. D.